

实时超声造影在评价冠心病患者左室整体与局部心功能中的价值

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[摘要] **目的:**探讨实时超声造影在评价冠心病患者左室整体与局部心功能中的价值。**方法:**对22名行冠脉旁路移植手术的患者进行实时心肌造影,分别于超声造影前后观察心内膜边界显示情况,评价节段室壁肌运动情况,测量左室射血分数并与X线左室造影测量结果进行比较。**结果:**超声造影后左室心内膜边界显示较造影前明显清晰,显示不清的节段减少,清晰显示的节段增多,记分指数增高($P < 0.05$)。造影前测量的左室射血分数与X线左室造影结果比较差异显著($P < 0.05$),相关性较低($r = 0.46, P < 0.05$);造影后测量的左室射血分数与X线左室造影结果无显著差异($P > 0.05$),且相关良好($r = 0.87, P < 0.01$)。在对节段室壁运动异常的检测中,以冠状动脉造影结果为标准,造影后检测灵敏度、特异度和准确度均高于造影前,分别为73.4%、70%、71.9%和55.2%、45.6%、50.9%($P < 0.05$)。**结论:**实时超声造影能有效增强左室心内膜边界显示和心肌显影,提高对左室整体和节段心功能检测的准确性。

[关键词] 实时超声造影;心室功能,左;冠状动脉心脏病

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Value of real-time contrast echocardiography in evaluation of global and regional left ventricular function in patients with coronary artery disease

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[ABSTRACT] **Objective:** To investigate the value of real-time contrast echocardiography in evaluation of global and regional left ventricular function in patients with coronary artery disease. **Methods:** Twenty-two patients receiving coronary artery bypass grafting(CABG) surgery were enrolled in this study. Before and after real-time contrast echocardiography, the left ventricular endocardial border, was delineated; the left ventricular ejection fraction (LVEF) was measured and the regional wall motion was assessed. LVEF results were compared with X-ray opacification reports. **Results:** After contrast enhancement, the endocardial border became more precise. The number of unclear endocardial border decreased while the number of clear border and the score index increased. The LVEF measured by echocardiography before contrast was significantly different from X-ray results($P < 0.05$), with a poor correlation ($r = 0.46, P < 0.05$). After contrast enhancement, the difference between these 2 methods became insignificant($P > 0.05$), with a good correlation ($r = 0.87, P < 0.05$). Meanwhile, the sensitivity, specificity and accuracy of echocardiography in detecting regional wall motion abnormalities were higher with contrast than those without (73.4%, 70%, 71.9% and 55.2%, 45.6%, 50.9%, respectively). **Conclusion:** Real-time contrast echocardiography can more precisely delineate left ventricular endocardial border and enhance the myocardial opacification, improving the accuracy in detection of the global and regional left ventricular function.

[KEY WORDS] real-time contrast echocardiography; ventricular function, left; coronary heart disease

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对左室整体收缩功能和节段室壁运动的评价是二维超声检查的重要内容。实时超声造影(real-time contrast echocardiography)是近年来发展的一项超声新技术,它使用稳定的能通过肺循环的微气泡造影剂,并通过特殊成像机制对造影剂进行检测。实时超声造影不仅能显著增强对心内膜边界的辨认,还能使心肌清晰显影,提高对整体和局部心功能判断的准确性。本研究采用这一方法对行冠状动脉旁路移植术(coronary artery bypass grafting, CABG)冠心病患者的心功能进行检测,拟了解实时

超声造影在评价心功能中的价值。

1 材料和方法

1.1 研究对象 2004年9月至2005年4月在我院胸心外科行冠脉旁路移植手术患者22名,男性18

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例,女性4例,年龄47~79岁,平均(62±9)岁。近期心肌梗死2例,陈旧性心肌梗死5例,不稳定心绞痛5例,其他10例为稳定型心绞痛,心功能Ⅱ~Ⅳ级。冠状动脉造影显示所有患者均存在直径狭窄>70%的病变,其中单支病变2例,2支病变6例,3支及以上病变14例。3例合并室壁瘤形成。排除心律失常、传导异常和严重瓣膜病变等疾患。

1.2 仪器设备

1.2.1 超声仪器 Siemens Acuson Sequoia-512型超声诊断仪,3V2c相控阵探头,频率2.5~4.0 MHz。该机具备谐波成像和对比脉冲序列(contrast pulse sequencing, CPS)成像系统,能进行低机械指数(mechanic index, MI)下的实时超声造影。造影剂采用Bracco公司生产的SoneVue,其内部充填高分子量惰性气体SF₆,外壳为磷脂,微泡密度1×10⁸~5×10⁸/ml。

1.2.2 X线检查 Siemens AXIOM Artis数字血管造影系统,造影剂为欧乃派克。

1.3 检测内容与方法

1.3.1 二维超声检查 分别记录胸骨旁左室长轴观,左室二尖瓣水平、乳头肌水平、心尖水平短轴观,心尖四腔、两腔观动态图像,存入磁光盘内,脱机进行分析。观察内容包括:(1)心内膜边缘显示情况。根据美国超声心动图学会推荐的16节段分析法和心内膜缘评分标准,0=完全不能显示;1=能模糊显示;2=清晰显示进行评分,并计算心内膜缘记分指数,为相关节段心内膜缘评分之和除以节段总数^[1]。(2)计算左室射血分数(left ventricular ejection fraction, LVEF)评价整体收缩功能。选取标准心尖四腔心切面图像,人工描绘心内膜轮廓,测量自二尖瓣环中点至心尖的左室长径,仪器自动以单平面Simpson法计算左室容积。分别测量左心室舒张末期容积(end diastolic volume, EDV)和收缩末期容积(end systolic volume, ESV),计算LVEF=(EDV-ESV)/EDV×100%。(3)观察节段室壁运动情况。测量各节段收缩末(Ts)、舒张末室壁厚度(Td)和心内膜位移幅度,计算室壁收缩增厚率 $\Delta T\%=(Ts-Td)/Td\times 100\%$,并对节段室壁运动进行半定量记分:运动正常,室壁运动的方向及幅度在正常范围,记1分;运动减弱(hypokinesis),室壁运动方向正常,幅度减小,室壁增厚率<25%,记2分;运动消失(akinesis),室壁收缩运动消失,局部节段无增厚改变,记3分;矛盾运动(dyskinesis)室壁收缩期运动方向与正常相反,收缩期室壁变薄,向心腔外膨出,记4分;合并室壁瘤记5分;显示不清,

难以判断的记为0分。

1.3.2 实时超声造影 选择CPS心肌造影成像模式,机械指数(mechanical index, MI)0.16,动态范围50 dB,增益0,差异增强3。将SoneVue粉剂(59 mg)与5 ml生理盐水混合后剧烈振摇20 s,得到白色、乳状的微泡混悬液。穿刺肘前静脉,使用20 G的静脉导管,抽取2.0 ml造影剂以1.0 ml/min的速度匀速推入静脉,用5 ml生理盐水冲洗。将左室心腔充分显影后各切面动态图像以及心肌充分显影后的动态图像分别存入磁光盘内,脱机进行分析。观察内容同二维超声检查。

1.3.3 X线检查 穿刺股动脉,置入F6鞘管,采用Judkins法进行多方位冠状动脉造影。然后经鞘管逆行置入猪尾造影导管至左心室,加压注射35~50 ml欧乃派克造影剂行左室造影测量射血分数。

1.4 统计学处理 结果用SPSS11.0软件包进行分析。记分等级数据比较采用Wilcoxon符号秩和检验,两两比较采用配对t检验,率的比较采用 χ^2 检验。检验结果P<0.05为相差显著,P<0.01为相差非常显著。

2 结果

2.1 超声造影前后左室心内膜边缘显示变化 造影剂经静脉注射后,在右室-左室-心肌内顺序显影,采用伪彩技术可观察到右室腔、左室腔内呈逐渐增强的亮黄色。左室腔显影后,心内膜边界显示较造影前明显清晰,部分完全不显示或模糊显示的节段变得显影清晰,心内膜缘记分由0分或1分增至2分,其中以侧壁、前壁以及心尖段心肌变化最为明显。造影后心内膜缘显示不清晰的节段数较造影前减少,清晰显示的节段数增加,心内膜缘记分指数增高(P<0.05)。见表1和图1。

表1 超声造影前后心内膜缘显示变化

Tab 1 Enhanced endocardial border by ultrasonic contrast

Group	Grading of regions			Score index
	[n(%)]			
	0	1	2	
Without contrast	64(18.2)	74(21.0)	214(60.8)	1.43
Post contrast	23(6.5)	49(13.9)	280(79.5)	1.73*

* P<0.05 vs without contrast

2.2 超声造影前后左室整体心功能变化(与X线左室造影比较) 分别于造影前后测量EDV、ESV并计算LVEF,并与X线左室造影的LVEF进行相关性比较。结果显示超声造影前测量的LVEF与X

线造影结果有统计学差异 ($P < 0.05$), 相关性较低 ($r = 0.46, P < 0.05$); 超声造影后 LVEF 值与 X 线

造影结果无统计学差异 ($P > 0.05$), 且相关良好 ($r = 0.87, P < 0.01$)。见表 2 和图 2。

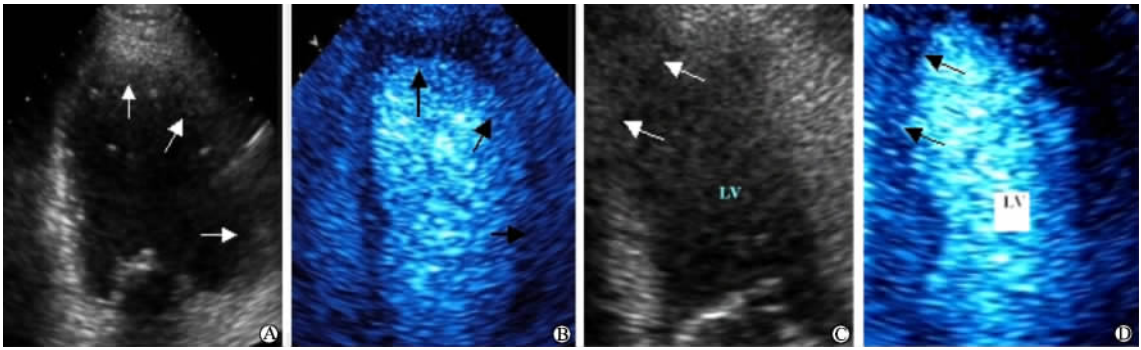


图 1 超声造影前后心内膜缘显示变化

Fig 1 Endocardial border before and after contrast

A, B: Apex four chamber view; C, D: Apex two chamber view; A, C: Before contrast, scoring 0; B, D: After contrast, scoring 2; A, B arrows: Endocardial border of lateral wall; C, D arrows: endocardial border of inferior wall; LV: Left ventricle

表 2 X 线左室造影与超声造影前后 LVEF 测值比较

Tab 2 Comparison of LVEF values between X-ray, before and after enhancement

Group	EDV (ml · m ⁻²)	ESV (ml · m ⁻²)	EF (%)
X-ray contrast	77.3 ± 17.1	38.2 ± 9.1	50.1 ± 9.2
Without ultrasonic contrast	80.6 ± 19.1	43.4 ± 9.7*	46.8 ± 11.6*
After ultrasonic contrast	76.2 ± 16.6	37.1 ± 9.4	49.2 ± 9.8

* $P < 0.05$ vs X-ray contrast

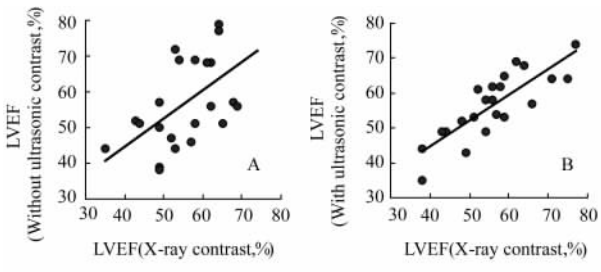


图 2 超声造影前后与左室造影 LVEF 相关性比较

Fig 2 EF value correlation between X-ray LV contrast and echocardiograph with and without contrast

2.3 超声造影前后对节段室壁运动的评价 左室造影后心肌逐渐显影, 随造影剂的进入心肌由暗黄色逐渐变为亮黄色, 造影后心肌各壁较造影前明显清晰(图 3), 显示不清的心肌节段数较造影前明显减少(表 3)。在对节段室壁运动的检测中, 以冠状动脉直径狭窄 > 70% 为标准, 造影前在狭窄冠状动脉供血的 192 个心肌节段中共检出室壁运动异常节段 106 个, 其中评为 2 分的节段 32 个, 3 分 40 个节

段, 4 分 14 个节段, 5 分 20 个节段; 判断为运动正常记 1 分的节段 38 个, 48 个节段显示不清记 0 分, 共漏检 86 个节段。在非狭窄相关节段中共检出 46 个节段室壁运动异常, 2 分 26 个节段, 3 分 14 个节段, 4 分 6 个节段, 另 41 个节段显示不清。造影后, 在狭窄相关节段中共检出室壁运动异常节段 141 个, 2 分 44 个节段, 3 分 54 个节段, 4 分 19 个节段, 5 分 24 个节段; 1 分 33 个节段, 0 分 18 个节段, 共漏检 51 个节段。非狭窄相关节段中检出室壁运动异常节段 29 个, 其中 2 分 16 个节段, 3 分 9 个节段, 4 分 4 个节段, 另 19 个节段显示不清为 0 分。以冠状动脉造影结果为标准, 造影后超声检测节段室壁运动异常的灵敏度、特异度和准确度均高于造影前, 分别为 73.4%、70%、71.9% 和 55.2%、45.6%、50.9% ($P < 0.05$)。见表 3。

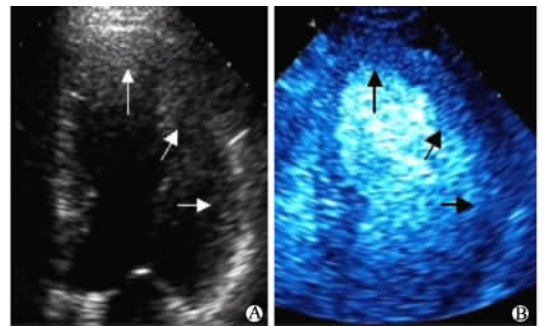


图 3 超声造影前后节段心肌显影变化(心尖四腔心切面)

Fig 3 Myocardium display before and after contrast (apex four chamber view)

A: Before contrast; B: After contrast; Arrows: Apical and myocardium of lateral wall

表 3 超声造影前后节段室壁运动检测与冠脉造影结果比较(节段数)

Tab 3 Detection of wall motion abnormality before and after ultrasonic contrast*

Coronary arteriography	Without contrast			Post contrast		
	Abnormal wall motion	Normal wall motion	Unsatisfied display	Abnormal wall motion	Normal wall motion	Unsatisfied display
Stenosis related regions	106	38	48	141	33	18
Non-stenosis regions	46	73	41	29	112	19
Total	152	111	89	170	145	37

*: Figures were the number of regions; coronary arteriography was taken as the golden standard

3 讨 论

尽管由于组织谐波的使用提高了信噪比、增强了二维超声图像的质量,但仍有 10%~20% 的患者左室心内膜边界显示得不满意,不能对左室功能作出准确的判断^[1]。近年来研究表明,对于部分成像困难的患者,使用造影剂能增强对心内膜边界的辨认,使对图像的分析更准确并具有可重复性^[2], Kuecherer^[3]报道了造影剂使左室腔显影,提高静息和峰值负荷时对心内膜边界的检出, Mulvagh 等^[4]研究表明实时心肌造影能极大地提高负荷试验的准确性,尤其是对于侧壁和前壁的心尖段的判断。

实时超声造影是新近发展的超声新技术,它使用稳定的能通过肺循环的微气泡造影剂,并通过造影特殊成像机制对微气泡进行检测。由于技术的进步使造影能在低能量下实现,它可以检测振动微泡的非线性反射而不需破坏微泡,从而实现实时成像。实时超声造影不仅能显著增强对心内膜边界的辨认,提高对整体和节段心功能判断的准确性,还可以准确定量节段微血管血流,在无创评价心肌活性方面具有广泛的应用前景^[5,6]。本研究采用第二代超声造影剂 SonoVue 以及对比脉冲序列 (contrast pulse sequencing, CPS) 成像技术和低机械指数 (mechanic index, MI) 对 22 名冠心病患者进行了实时超声造影,并重点探讨该技术在提高患者整体和节段心功能检测中的价值。

SonoVue 是第二代造影剂的代表,为磷脂外壳包裹的惰性气体 SF₆,理化性质稳定,与注射用水充分混合振摇后形成的微气泡造影剂平均直径仅 2.5 μm,变形性与红细胞相当,能通过肺循环进入左室心腔以及冠脉循环,当通过心肌时完全保持在毛细血管内,从而可以实现心腔显影和心肌显影。SonoVue 微泡外壳具有良好的弹性,在低机械指数状态下也能产生明显的谐波信号且不被破坏,适宜

用于实时成像^[7,8]。

提高微气泡敏感性的非线性超声技术是实现实时造影的关键。以本研究中使用的对比脉冲序列 (contrast pulse sequencing, CPS) 成像技术为例,它顺序发射一个序列的正向和反向脉冲,由于周围组织的线性作用,叠加后的脉冲信号互相抵消为 0,而微泡振动的非线性作用使回波信号明显增强,可选择性提高造影剂微泡的敏感性,增强心肌显像和心内膜边缘显示能力^[9]。另外如其他仪器使用的能量调制技术、脉冲反向多普勒技术、多脉冲处理技术等,都能明显提高信噪比,显著提高检测造影剂的灵敏性,使心肌造影显像更加清晰真实。

低机械指数是实时造影的另一关键技术,本研究中使用的 MI 为 0.16~0.20,它不仅提供了更均匀的能量场,使造影剂在整个扇区内分布均匀,心内膜边界显示更加清晰,还使超声能量对造影剂的破坏减少到最低,使造影剂持续停留在微血管内,不间断地连续实时成像。同时,由于组织谐波和其他的非线性信号要在高能量下产生,当能量极低时组织几乎不产生非线性信号,从而能选择性地滤过本底提高信噪比,增强心肌造影效果^[10]。

本研究综合使用上述技术对冠心病患者成功进行了实时造影,结果显示造影后心内膜边界显示较造影前明显清晰,超声测量的 LVEF 与 X 线左室造影的检测结果较造影前更为接近,且具有更高的相关性,对整体心功能检测的准确性明显提高。在对节段心肌运动的检测中,造影后对心内膜运动幅度的观察更为灵敏,心肌的清晰显影使室壁增厚率的测量更加准确,从而极大地提高了对节段室壁运动异常的检测的准确性。另外,由于实时心肌造影在无创评价心肌活性方面的作用,该技术将在冠心病的诊断和治疗评价中具有越来越重要的临床价值。

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Inhibitory effect of recombinant adenovirus carrying melittin gene on hepatocellular carcinoma

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[ABSTRACT] Objectives: To search for a new clinical application of melittin (Mel); treating hepatocellular carcinoma with Mel gene. **Methods:** Recombinant adenoviruses carrying the Mel gene and alpha-fetoprotein (AFP) promoter (Ad-rAFP-Mel) were constructed through a bacterial homologous recombinant system. The efficiency of adenovirus-mediated gene transfer and the inhibitory effect of Ad-rAFP-Mel on the proliferation of hepatocarcinoma cells were determined by X-gal stain and MTT assay, respectively. The tumorigenicity of hepatocarcinoma cells transfected by Ad-rAFP-Mel and the antitumor effect of Ad-rAFP-Mel on transplanted tumor in nude mice were detected *in vivo*. **Results:** The Mel mRNA was transcribed in BEL-7402 hepatocellular carcinoma cells transduced by Ad-rAFP-Mel. The efficiency of adenovirus-mediated gene transferred to BEL-7402 cells was 100% when the multiplicity of infection of Ad-rAFP-Mel was 10 *in vitro*, and was also high *in vivo*. The inhibitive rates of Ad-rAFP-Mel and Ad-rAFP for BEL7402 cells were $(66.2 \pm 2.7)\%$ and $(2.9 \pm 2.3)\%$ ($t = 30.83$, $P = 6.6 \times 10^{-6}$) by MTT assay. The inhibitive rates of Ad-CMV-Mel for BEL7402, SMMC7721 and L02 cells were $(58.9 \pm 9.6)\%$, $(65.9 \pm 3.8)\%$ and $(31.7 \pm 1.2)\%$, respectively, and of Ad-rAFP-Mel were $(66.2 \pm 2.7)\%$, $(16.1 \pm 6.6)\%$ and $(7.5 \pm 3.3)\%$, respectively ($t = 1.27$, $P = 0.27$; $t = 11.31$, $P = 3.5 \times 10^{-4}$; and $t = 12.12$, $P = 2.7 \times 10^{-4}$ versus the Ad-CMV-Mel group in the same cells). The tumorigenicity rates of hepatocarcinoma cells transfected by Ad-rAFP-Mel were decreased. A significant antineoplastic effect was detected on transplanted tumor in nude mice by intratumoral injection of Ad-rAFP-Mel. **Conclusions:** Ad-rAFP-Mel can inhibit specifically proliferation of AFP-producing human hepatocarcinoma cells *in vitro* and *in vivo*. This suggests that animal toxin gene can be used as an antitumor gene.

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